

EXHIBIT O

Cancer Mortality in Relation to Environmental Chromium Exposure

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From the 1950s to the 1980s, hexavalent chromium compounds were used as additives at certain water-cooling towers at three southern California gas compressor facilities. Claims of potential residential chromium exposure prompted the examination of age-adjusted mortality rates during 1989 to 1998 for lung cancer, all cancer, and all deaths for neighborhoods near versus distant from the plants. Differences in the rates between areas tended to be small and not statistically significant. The only significant difference was a lower, rather than higher, rate of total cancer among women in the potentially exposed areas. Study limitations preclude a definitive assessment of risk, but similar to previous investigations of cancer in relation to environmental chromium exposure in other locations, this study found no evidence of a cancer hazard among residents living near these California gas compressor facilities. (J Occup Environ Med. 2001;43:635–640)

Exhibit

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Chromium is a ubiquitous compound found in animals, plants, rocks, soil, and air. The two most stable forms are trivalent chromium (III) and hexavalent chromium (VI). In humans and animals, trivalent chromium is an essential element important for the metabolism of glucose, fat, and protein, and the compounds have some commercial uses.¹ Hexavalent chromium is used in many industrial processes, including corrosion inhibition, leather tanning, chrome plating, stainless steel production, glassware-cleaning solutions, wood preservatives, and various pigments.^{1–3} Although the evidence for the carcinogenicity of trivalent chromium is lacking, hexavalent chromium is classified as a human carcinogen by the International Agency for Research on Cancer and the US Environmental Protection Agency, based on excess lung cancer found in workers involved in chromate and chromate pigment production and in the chromium plating industries.^{3,4}

Soluble hexavalent chromium compounds were used as cooling water tower additives from the 1950s up to the 1980s at certain gas compressor plants operated by the Pacific Gas and Electric Company (PG&E) in Kettleman, Hinkley, and Topock, California. Heated pipes from the gas compressor plant were placed in water troughs to prevent overheating. Chromium compounds were added to the water to inhibit corrosion of the pipes. Wastewater from the cooling towers was disposed of in ponds near the plants, and some compounds eventually flowed into the water table.

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Concern over the potential for residential exposure to chromium from the Hinkley plant and the possibility of adverse health effects led to litigation against PG&E, which was settled in 1996 and recently was the subject of the popular film *Erin Brockovich*.

Given these concerns, we were asked by PG&E to conduct a study of mortality among residents in the areas surrounding the Hinkley and in two other gas-generating facilities where chromium compounds were used. We sought to determine if lung cancer, all types of cancer, and mortality in general occurred in excess for area residents.

Methods

Zip codes encompassing Kettleman City, Hinkley, and Topock were identified with Geographic Information System software⁵ and were used to define the potentially exposed areas, designated henceforth as KHT areas (Fig. 1). The zip codes for a sample of residents in litigation were reviewed to ensure that their zip codes were accounted for in the KHT areas. For comparison, non-KHT areas were defined as areas covered by the remainder of zip codes in Kings County or San Bernardino County (Fig. 1). The populations of the KHT and non-KHT areas were determined from 1990 US Census data.⁶

The numbers of residents of the two counties who died during 1989 to 1998 from lung cancer, all types of cancer, and all causes of mortality were abstracted from the California Death Statistical Master file.⁷ Only those deaths with a valid zip code in the file were included in the analysis. Deaths from each outcome of interest were determined for the KHT and non-KHT areas.

From the census and mortality data, age-adjusted rates of mortality for lung cancer, all cancer combined, and all causes of death combined were computed for men and women separately and combined in the KHT and non-KHT areas. Standard errors of the age-adjusted rates and 95%

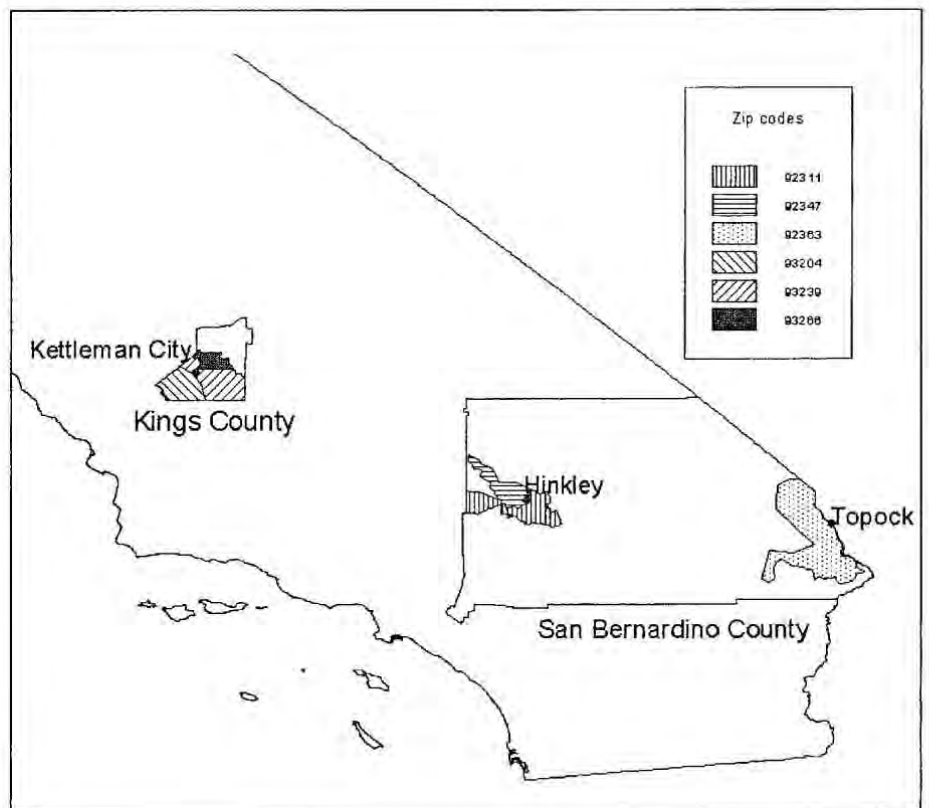


Fig. 1. Zip codes surrounding Kettleman City, Hinkley, and Topock, California.

confidence intervals (CI) were calculated.⁸ The age-adjusted rates in KHT areas were compared with those in non-KHT areas by calculating rate ratios (RRs) and 95% CIs around the RR.⁹

Results

We reviewed the county of residence for all persons who died in the state of California from 1989 to 1998 (2,226,214 deaths). County of residence of death was recorded for all records. A total of 107,893 deaths occurred among residents of San Bernardino County and Kings County combined. Of these records, 80 people were excluded because of a missing date of birth, and 586 people were excluded because of a missing zip code at time of death. The remaining 107,227 deaths were the focus of this analysis.

The age-adjusted rates for KHT areas and non-KHT areas and the RRs and 95% CIs for lung cancer

mortality, all cancer mortality, and all mortality are described in Table 1. The RR of lung cancer in men (RR = 0.98; 95% CI, 0.83 to 1.16), women (RR = 1.06; 95% CI, 0.87 to 1.30), and both genders combined (RR = 1.03; 95% CI, 0.90 to 1.17) was near 1.0, indicating that the mortality rates in KHT areas were similar to the rates in non-KHT areas, with none of the differences between areas being statistically significant. Similarly, the rates of all cancer combined were also near 1.0 for men (RR = 0.96; 95% CI, 0.87 to 1.06) and both genders combined (RR = 0.93; 95% CI, 0.87 to 1.00). However, women in KHT areas were statistically significantly less likely to die from cancer than women in non-KHT areas (RR = 0.87; 95% CI, 0.78 to 0.97). Men, women, and both genders combined experienced similar rates of mortality for all causes of death in KHT areas and non-KHT areas, as all of the RRs were near 1.0.



TABLE 1

Age-Adjusted Rates, RRs, and 95% CIs for Lung Cancer, All Cancer Combined and All Mortality in KHT and Non-KHT Areas, 1989–1998*

	KHT Areas†			Non-KHT Areas†			Relative Rate	95% CI
	No. of Deaths	Rate§	95% CI	No. of Deaths	Rate§	95% CI		
Lung cancer								
Men	147	59	49–68	3,754	60	58–62	0.98	0.83–1.16
Women	97	45	36–54	2,580	42	41–44	1.06	0.87–1.30
Both	244	53	46–59	6,334	51	50–53	1.03	0.90–1.17
All cancer								
Men	438	179	162–196	11,677	186	183–190	0.96	0.87–1.06
Women	327	152	135–169	10,728	175	172–179	0.87	0.78–0.97
Both	765	169	157–181	22,405	181	179–184	0.93	0.87–1.00
All mortality								
Men	2,045	826	791–860	54,486	852	845–859	0.97	0.93–1.01
Women	1,604	797	759–836	49,092	812	805–819	0.98	0.93–1.03
Both	3,649	820	794–846	103,578	833	829–838	0.98	0.95–1.02

* RR, rate ratio; CI, confidence interval; KHT, Kettleman City, Hinkley, and Topock.

† KHT areas include the following zip codes: 93266, 93239, 93204, 92363, 92347, 92311.

‡ Non-KHT areas include all other zip codes in San Bernardino and Kings Counties.

§ Per 100,000 person-years.

Discussion

Although it is difficult to draw etiologic inferences from a simple comparison of mortality rates between areas, the results of this study are reassuring because they indicate that rates of cancer generally, and lung cancer in particular, are not higher in KHT than in non-KHT areas. The time segment studied (1989 to 1998) covered a period from more than 5 to up to nearly 50 years after chromium compounds were used in the gas compressor facilities in the KHT areas, allowing an extensive latency period for a cancer excess to be expressed had it existed.

Evidence documenting an association between chromium and human lung cancer derives from epidemiologic studies of occupational groups heavily exposed to hexavalent compounds. Increased risks of lung cancer have been found fairly consistently in chromate production, chromate pigment production, and chromium plating industries—industries where hexavalent forms were used, sometimes with high levels of worker exposure.^{2,3} Improvements in the production process and industrial hygiene over the past 30 to 40 years,

however, have substantially reduced the workers' exposure to hexavalent chromium and, consequently, the risk for lung cancers in these industries.¹⁰ Evidence of a cancer hazard in industries where chromate is used (such as stainless steel, ferrochromium alloy, aircraft manufacturing, and leather tanning) rather than produced is less conclusive.^{2,3} Indeed, over the past decade occupational studies of aircraft workers involved in spray painting and other jobs involving hexavalent chromium exposure have found no increase in lung cancer.^{11,12}

Before conducting the present study of mortality rates among residents of KHT areas, we performed an occupational cohort mortality study among male PG&E employees, including those who had worked at the three gas compressor facilities.¹³ There was no evidence of an excess of total cancer (RR = 0.89; 95% CI, 0.87 to 0.91), lung cancer (RR = 0.98; 95% CI, 0.92 to 1.05), or any other site-specific cancer among PG&E workers overall, nor among those who had worked or trained at the gas compressor plants. The risk of lung cancer did not increase with length of employment or

time since hired, providing further evidence of a lack of association between employment and cancer. The study indicated that air and waterborne chromate exposures at these facilities were not high enough to result in an increased risk of cancer among the workers.

Occupational studies have been the mainstay of medical research to identify and quantify the risks of cancer and other diseases associated with chemical exposures.¹⁴ Workers handling, breathing, or ingesting various compounds are typically exposed at much higher levels than the general population and can be seen as sentinels of risk if it exists. The greater range of on-the-job exposures provides the opportunity to assess not only whether an increase in risk has occurred, but also to examine potential dose-response relationships. Data from occupational studies can then be used to project whether lower-level general population exposures to the chemical agent may convey some added risk. On the basis of the absence of increased cancer risk among PG&E workers,¹³ no excess would be predicted for residents of the communities surrounding the KHT plants. Neverthe-



less, we were commissioned to examine cancer rates for the neighboring populations in an attempt to directly assess this possibility. We found no evidence of excess cancer risks among residents of the zip codes closest to the gas compressor facilities.

Similar to our research, several studies have examined cancer mortality in relation to residence near industrial sites that produced or used chromium products. A Swedish study determined the rates of lung cancer in residents near two ferro-alloy plants.¹⁵ The investigators calculated the lung cancer mortality rate in the two communities near the plants to the rate in the rest of the county, and the lung cancer mortality rate in the country of Sweden as a whole. The rates were similar for both male and female residents near the plants compared with rates for the comparison groups.

Investigators in China compared cancer mortality in five communities near the Jinzhou Alloy Plant, a chromium production plant, with residents in the province as a whole. An early report claimed that mortality overall and from lung cancer and stomach cancer were higher in the areas near the plant compared with mortality in the whole district.¹⁶ However, a follow-up report by the same study group discounted these findings.¹⁷ The authors could find no clear statistical increase in cancer mortality overall or for lung and stomach cancers. In fact, cancer rates were lower in the communities with higher levels of hexavalent chromium in wells that supplied the communities' water, suggesting that life-style or environmental factors not related to the hexavalent chromium contaminated water were important contributory factors.

In Nebraska, no apparent association between environmental chromium and cancer mortality was evident across 453 communities with a greater than 10-fold variation in average chromium levels in drinking water.¹⁸ In Canada, on-site chro-

mium in drinking water was hypothesized to be related to several cancers among asbestos miners, but a case review suggested no effect of chromium exposure and indicated that the scientific literature provided no evidence of a cancer hazard from oral exposure to chromium.¹⁹

Some investigations have evaluated levels of chromium in household and/or biologic samples in the neighborhoods of industrial facilities that have used chromium compounds, or wastes sites that have stored them. Elevated levels of total chromium have been found in household dust, in residents' urine and hair, and near factories and waste sites in New Jersey, Mexico, and China, but measures of cancer risk or other health status were generally not reported.²⁰⁻²⁴ In a review of exposures from chromium-containing landfills in New Jersey and elsewhere, one projection concluded that no health hazard was posed from either acute or chronic exposure.²⁵

In the United Kingdom, there were perceptions of increased health risk among persons who lived near a chromium-contaminated waste site, but little difference in systematically obtained self-reported health status was found between residents near the waste site versus residents of an uncontaminated control area.²⁶ The authors indicated that the similar health patterns suggested no evidence of harm, despite anxiety related to people's beliefs about potential adverse health effects. In a recent review of the effects of environmental chromium exposures in the United Kingdom, no clear evidence of adverse health outcomes were noted in either the overall general population or in subgroups exposed around industrialized or contaminated sites.²⁷

Our study assessing mortality among residents near versus distant from gas compressor plants where chromium additives were used likewise found no difference in lung or total cancer mortality, consistent with the lack of effect seen in investigations elsewhere. In a prior case

report, Bick et al²⁸ described two cases of Hodgkin's disease among residents of Hinkley, with the authors suggesting that the cluster may have been due to environmental chromium contamination and that the overall cancer risks following exposure to chromium may be increased nearly 80-fold. Case reports such as this are no substitute for systematic epidemiologic study, and no inferences can be drawn from the Bick et al²⁸ report or its literature review, the adequacy of which was recently questioned.¹⁹ Had there actually been an 80-fold excess of cancer in the areas we studied, it surely would have been detected; the upper 95% CI in Table 1 indicate that even rather small increases in cancer in KHT areas can be ruled out. We are aware of no other studies suggesting that chromium exposure could result in an 80-fold increase in overall cancer.²⁻⁴ Although a few authors have noted some associations between chromium exposure and several types of cancer,²⁹ the scientific consensus of evidence indicates that chromium carcinogenicity is specific for respiratory cancer following heavy exposure to hexavalent compounds in the work environment. Indeed, the International Agency for Research on Cancer review states that "for cancers other than of the lung and sinonasal cavity, no consistent pattern of excess risk has been shown among workers exposed to chromium compounds".³ Similarly, the US Environmental Protection Agency notes that the major target organ for carcinogenicity is the respiratory tract (following hexavalent chromium inhalation) and that there is "no evidence that chromium has the potential to cause cancer from lifetime exposures in drinking water".⁴ Biologic support exists for such pronouncements, because hexavalent chromium is reported to be rapidly and substantially detoxified in the body when orally ingested.³⁰

The present study, an ecologic survey, has several limitations common



to this type of investigation. First, we had no information on environmental, lifestyle, medical, or other characteristics of individuals with cancer or other causes of death in the KHT or non-KHT areas; our data included only the area-wide mortality rates. The estimated area population sizes during the 1989-to-1998 study period were based on the 1990 census population. If the population of the KHT or non-KHT areas had changed dramatically since 1990, then the RRs could be affected. We had no small-area quantitative measures of population growth, but personal communication with the postmasters in the KHT areas revealed that the population had not changed greatly.

Our analyses of geographic areas relied on postal zip codes recorded in the California Death Statistical Master file. Although the KHT area included the zip codes surrounding the gas compressor plants, some of the zip codes encompassed large locales and, consequently, residences not adjacent to the facilities. In particular, the zip code that included Topock was quite large. On the other hand, some cancer cases may have been missed by not including one zip code south of Hinkley. Analyses performed without including Topock or the excluded zip code in the KHT areas, however, resulted in no material changes. We were also concerned about the influence of zip code 92311, which included the city of Barstow, on the death rates in the KHT area. Again, after excluding this zip code, we found no evidence of an increase in lung cancer, all cancer combined, or all mortality in the KHT areas.

We are unable to make any conclusions regarding the median, average, or cumulative levels of hexavalent or total chromium exposure among residents in the KHT versus non-KHT areas under study.

We examined cancer mortality, not cancer incidence. Mortality studies have been the primary means of identifying occupational and environmental carcinogens in epidemiol-

ogy. They generally provide valid measures of relative risk, even for cancers with relatively good survival, although the statistical power of mortality studies will be reduced for cancers with high survival rates. However, the median survival time for patients diagnosed with lung cancer, the cancer of primary concern when hexavalent chromium exposure is suspected, is relatively short, so mortality rates and incidence rates for this cancer are essentially equivalent.

In summary, this study found no evidence that persons living in postal codes near gas compressor plants are experiencing higher death rates due to cancer overall or lung cancer specifically. Furthermore, the mortality rate for all causes of death in KHT areas was not different than the rate for non-KHT areas. This study suggests that the health of residents in and around Kettleman City, Hinkley, and Topock is similar to the health of residents in the rest of Kings County and San Bernardino County.

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Longevity

Estimated number of Americans who are at least 100 years old (a 130% increase from 1990): 67,000.

Projected number of centenarians in 2050: 834,000.

Centenarians who are women: 82%.

Life expectancy at birth in 1900: 46 (men) and 48 (women).

Life expectancy at birth in 1997: 74 (men) and 80 (women).

Portion of earnings that must be saved every year to maintain preretirement income when starting work at 20, retiring at 60, and living to 100: 31%.

—From Rheault M. The Kiplinger Monitor. *Kiplinger's Personal Finance*. 2001;55(3):28.

